



Attorney Docket No. 9233-54

1615

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re: Ekwuribe et al.  
Serial No.: 09/873,899  
Filed: June 4, 2001  
For: *MIXTURES OF INSULIN DRUG-OLIGOMER CONJUGATES COMPRISING POLYALKYLENE GLYCOL, USES THEREOF, AND METHODS OF MAKING SAME*

Confirmation No.: 5139  
Group Art Unit: 1615

#11

Date: January 10, 2003

Commissioner for Patents  
Washington, DC 20231

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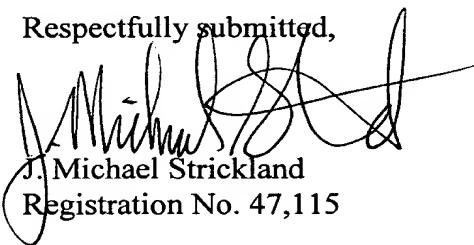
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**INFORMATION DISCLOSURE STATEMENT**

Sir:

Attached is a form PTO-1449, together with a copy of the identified document(s). This Information Disclosure Statement is submitted in accordance with 37 C.F.R. § 1.97(b), within three months of the filing date of the above-referenced application or before the mailing of a first Office Action on the merits, whichever event occurs last. Accordingly, no fee is required. The Commissioner is authorized to charge any additional fee, or credit any refund, to our Deposit Account No. 50-0220.

Respectfully submitted,



J. Michael Strickland  
Registration No. 47,115

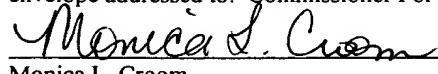


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FORM PTO-1449 U.S. Department of Commerce Patent and Trademark Office				Attorney Docket Number 9233-54			Serial No. 09/873,899
LIST OF DOCUMENTS CITED BY APPLICANT  <i>OIPR</i> JAN 13 2003 PATENT & TRADEMARK OFFICE				Applicants: Ekwuribe et al.			
				Filing Date: 06/04/01		Group 1615	
U. S. PATENT DOCUMENTS							
Examiner Initial		Document Number	Date	Name	Class	Subclass	Filing Date if Appropriate
<i>JR</i>	1.	3,919,411	11/11/75	Glass et al.	424	78,27	
<i>JR</i>	2.	3,256,153	06/14/66	Heimlech	424	497	
<i>JR</i>	3.	3,868,356	02/25/75	Smyth	530	303	
<i>JR</i>	4.	3,950,517	04/13/76	Lindsay et al.	514	3	
<i>JR</i>	5.	4,003,792	01/18/77	Mill et al.	530	303	
<i>JR</i>	6.	4,044,196	08/23/77	Huper et al.	526	271	
<i>JR</i>	7.	4,087,390	05/02/78	Shields	525	54,11	
<i>JR</i>	8.	4,093,574	06/06/78	Shields	525	54,11	
<i>JR</i>	9.	4,100,117	07/11/78	Shields	525	54,11	
<i>JR</i>	10.	4,229,438	10/21/80	Fujino et al.	514	15	
<i>JR</i>	11.	4,253,998	03/03/81	Sarantakis	525	54,11	
<i>JR</i>	12.	4,277,394	07/07/81	Fujino et al.	530	330	
<i>JR</i>	13.	4,338,306	07/06/82	Kitao et al.	514	4	
<i>JR</i>	14.	4,348,387	09/07/82	Brownlee et al.	514	4	
<i>JR</i>	15.	4,410,547	10/18/83	Ueno et al.	514	557	
<i>JR</i>	16.	4,469,681	09/04/84	Brownlee et al.	514	4	
<i>JR</i>	17.	4,472,382	09/18/84	Labrie et al.	514	15	
<i>JR</i>	18.	4,554,101	11/19/85	Hopp	514	17	
<i>JR</i>	19.	4,579,730	04/01/86	Kidron et al.	514	3	
<i>JR</i>	20.	4,585,754	04/29/86	Meisner et al.	514	8	
<i>JR</i>	21.	4,622,392	11/11/86	Hong et al.	536	26,22	
<i>JR</i>	22.	4,684,524	08/04/87	Eckenhoff et al.	424	469	
<i>JR</i>	23.	4,698,264	10/06/87	Steinke	428	402,2	
<i>JR</i>	24.	4,717,566	01/05/88	Eckenhoff et al.	424	438	
<i>JR</i>	25.	4,744,976	05/17/88	Snipes et al.	424	408	

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26.	4,772,471	09/20/88	Vanlerberghe et al.	424	450	
27.	4,797,288	01/10/89	Sharma et al.	424	476	
28.	4,839,341	06/13/89	Massey et al.	514	4	
29.	4,840,799	06/20/89	Applegren et al.	424	493	
30.	4,849,405	07/18/89	Ecanow	514	3	
31.	4,917,888	04/17/90	Katre et al.	424	85.91	
32.	4,935,246	06/19/90	Ahrens	424	490	
33.	4,946,828	08/07/90	Markussen	514	3	
34.	4,957,910	09/18/90	Sutton et al.	514	182	
35.	4,963,367	10/16/90	Ecanow	424	485	
36.	4,994,439	02/19/91	Longenecker et al.	514	3	
37.	5,013,556	05/07/91	Woodle et al.	424	450	
38.	5,055,300	10/08/91	Gupta	424	409	
39.	5,055,304	10/08/91	Makino et al.	424	465	
40.	5,089,261	02/18/92	Nitecki et al.	424	85.2	
41.	5,093,198	03/03/92	Speaker et al.	428	402.21	
42.	5,157,021	10/20/92	Balschmidt et al.	514	3	
43.	5,162,430	11/10/92	Rhee et al.	525	54.1	
44.	5,164,366	11/17/92	Balschmidt et al.	514	3	
45.	5,202,415	04/13/93	Jonassen et al.	550	303	
46.	5,206,219	04/27/93	Desai	514	3	
47.	5,283,236	02/01/94	Chiou	514	2	
48.	5,286,637	02/15/94	Veronese et al.	435	183	
49.	5,304,473	04/19/94	Belagaje et al.	435	69.7	
50.	5,312,808	05/17/94	Shorr et al.	514	6	
51.	5,405,621	04/11/95	Sipos	424	490	
52.	5,415,872	05/16/95	Sipos	424	490	
53.	5,438,040	08/01/95	Ekwuribe	514	3	

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54.	5,444,041	08/22/95	Owen et al.	514	2	
55.	5,457,066	10/10/95	Frank et al.	435	68,1	
56.	5,461,031	10/24/95	De Felippis	514	4	
57.	5,468,478	11/21/95	Saifer et al.	424	78.27	
58.	5,504,188	04/02/96	Baker et al.	530	304	
59.	5,506,203	04/09/96	Backstrom et al.	514	4	
60.	5,518,998	05/21/96	Backstrom et al.	514		
61.	5,523,348	06/04/96	Rhee et al.	525	54.1	
62.	5,529,915	06/25/96	Phillips et al.	435	188	
63.	5,545,618	08/13/96	Buckley et al.	514	12	
64.	5,606,038	02/25/97	Regen	536	6.5	
65.	5,612,460	03/18/97	Zalipsky	530	391.9	
66.	5,631,347	05/20/97	Baker et al.	530	303	
67.	5,637,749	06/10/97	Greenwald	558	6	
68.	5,646,242	07/08/97	Baker et al.	530	303	
69.	5,650,388	07/22/97	Shorr et al.	514	6	
70.	5,658,878	08/19/97	Backstrom et al.	514	3	
71.	5,681,811	10/28/97	Ekwuribe	514	8	
72.	5,693,609	12/02/97	Baker et al.	514	3	
73.	5,693,769	12/02/97	Kahne et al.	536	5	
74.	5,700,904	12/23/97	Baker et al.	530	305	
75.	5,707,648	01/13/98	Yiv	424	450	
76.	5,738,846	04/14/98	Greenwald et al.	424	85.7	
77.	5,747,445	05/05/98	Backstrom et al.	514	4	
78.	5,747,642	05/05/98	De Felippis	530	304	
79.	5,750,497	05/12/98	Havelund et al.	514	3	
80.	5,766,620	06/16/98	Heiber et al.	424	436	
81.	5,824,638	10/20/98	Burnside et al.	514	3	

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		Filing Date: 06/04/01	Group 1615

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82.	5,830,853	11/03/98	Backstrom et al.	514	4	
83.	5,830,918	11/03/98	Sportsman et al.	514	648	
84.	5,849,860	12/15/98	Hakimi et al.	528	370	
85.	5,853,748	12/29/98	New	424	439	
86.	5,854,208	12/29/98	Jones et al.	514	3	
87.	5,856,451	01/05/99	Olsen et al.	530	402	
88.	5,866,538	02/02/99	Norup et al.	514	3	
89.	5,898,028	04/27/99	Jensen et al.	514	4	
90.	5,902,588	05/11/99	Greenwald et al.	424	278.1	
91.	5,905,140	05/18/99	Hansen	530	303	
92.	5,907,030	05/25/99	Shen et al.	530	331	
93.	5,922,675	07/13/99	Baker et al.	514	4	
94.	5,942,248	08/24/99	Barnwell	424	457	
95.	5,948,751	09/07/99	Kimer et al.	514	4	
96.	5,952,008	09/14/99	Backstrom et al.	424	499	
97.	5,952,297	09/14/99	De Felippis et al.	514	3	
98.	5,962,267	10/05/99	Shin et al.	435	69.4	
99.	5,968,549	10/19/99	New et al.	424	450	
100.	5,969,040	10/19/99	Hallahan et al.	525	54.1	
101.	5,981,709	11/09/99	Greenwald et al.	530	351	
102.	5,985,263	11/16/99	Lee et al.	424	85.2	
103.	6,004,574	12/21/99	Backstrom et al.	424	434	
104.	6,025,325	02/15/00	Campfield et al.	514	2	
105.	6,034,054	03/07/00	De Felippis et al.	514	34	
106.	6,043,214	03/28/00	Jensen et al.	514	3	
107.	6,051,551	04/18/00	Hughes et al.	514	3	
108.	6,063,761	05/16/00	Jones et al.	514	3	
109.	6,093,391	07/25/00	Kabanov et al.	424	85.1	

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110.	6,113,906	09/05/00	Greenwald et al.	424	194.1	
111.	6,165,976	12/26/00	Backstrom et al.	514	3	
112.	6,177,087	01/23/01	Greenwald et al.	424	278.1	
113.	6,191,105	02/20/01	Ekwuribe et al.	514	3	
114.	6,200,602	03/13/01	Watts et al.	424	463	
115.	6,211,144	04/03/01	Havelund	514	4	
116.	6,248,363	06/19/01	Patel et al.	424	497	
117.	6,251,856	06/26/01	Markussen et al.	514	3	
118.	6,258,377	07/10/01	New et al.	424	450	
119.	6,268,335	07/31/01	Brader	514	3	
120.	6,306,440	10/23/01	Backstrom et al.	424	499	
121.	6,309,633	10/30/01	Ekwuribe et al.	424	85.1	
122.	6,310,038	10/30/01	Havelund	514	4	
123.	6,335,316	01/01/02	Hughes et al.	514	3	

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	Document Number	Date	Country	Class	Subclass	Translation Yes   No
124.	GB 1 492 997	11/23/77	Great Britain			Yes
125.	EP 0 031 567	07/08/81	EPO			Yes
126.	JP 1 254 699	10/11/89	Japan			No
127.	WO 93/01802	02/04/93	PCT			Yes - abstract
128.	WO 95/09831	04/13/95	PCT			Yes
129.	WO 95/30641	11/16/95	PCT			Yes
130.	EP 0 597 007	10/16/96	EPO			Yes
131.	WO 98/07745	02/26/98	PCT			Yes

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132.	Abuchowski, A. and F. F. Davis, "Soluble Polymer-Enzyme Adducts," pp. 368-383, Enzymes as Drugs, J. S. Holcnenberg, John Wiley, 1981.
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		Filing Date: 06/04/01	Group 1615
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133.	Akiyama, M. et al., "The Synthesis of New Derivatives of 1-.beta.-D-Arabinofuranosylcytosine," <i>Chem. Pharm. Bull.</i> , 1978, 26(3): p. 981-984.		
134.	Aoshima, M. et al., "N.sup.4 -Behenoyl-1-.beta.-D-Arabinofuranosylcytosine as a Potential New Antitumor Agent," <i>Cancer Research</i> , 1977, 37: pp. 2481-2486.		
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136.	Banting et al., "Pancreatic Extracts in the Treatment of Diabetes Mellitus: Preliminary Report," <i>Can. Med. Assoc. J.</i> , 145(10): 1281-1286 (1991).		
137.	Baudys et al., "Stabilization and Intestinal Absorption of Human Calcitonin," <i>J. Contr. Rel.</i> , 39: 145-51 (1996).		
138.	Baudys, M. et al., "Synthesis and Characterization of Different Glycosylated Derivatives of Insulin" <i>Proceed. Intern. Symp. Cont. Rel. Bioactive. Mater.</i> , 1992, 19: 210-211.		
139.	Bocci, E. et al., "Pharmacokinetic Properties of Polyethylene Glycol Derivatized Superoxide Dismutase," <i>Pharm. Res. Comm.</i> , 1982 14: 113-120.		
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141.	Brange, J. et al, "Chemical Stability of Insulin. 1. Hydrolytic Degradation During Storage of Pharmaceutical Preparations," <i>Pharm. Res.</i> , 1992, 9 (6): 715-726.		
142.	Brange, J. et al, "Chemical Stability of Insulin. 2. Formation of Higher Molecular Weight Transformation Products During Storage of Pharmaceutical Preparations," <i>Pharm. Res.</i> , 1992, 9 (6) 727-734.		
143.	Chien, Y. W., Novel Drug Delivery Systems, pp. 678-679, Marcell Decker, Inc., New York, N.Y., 1992.		
144.	Conradi, R.A., et al., "The Influence of Peptide Structure on Transport Across Caco-2 Cells," <i>Pharm. Res.</i> , 1991, 8(12): 1453-1459.		
145.	Delgado et al.; "The Uses and Properties of PEG-Linked Proteins" <i>Critical Reviews in Therapeutic Drug Carrier Systems</i> 9:3,4 249-304 (1992).		
146.	Engel et al.; "Insulin: Intestinal Absorption as Water-in-Oil-in-Water Emulsions" <i>NATURE</i> 219 856-857 (1968).		
147.	Fasano, Alessio; "Innovative strategies for the oral delivery of drugs and peptides" <i>TIBTECH</i> 16 152-157 (1998).		
148.	Forst et al., "New Aspects on Biological Activity of C-peptide in IDDM Patients," <i>Exp. Clin. Endocrinol. Diabetes</i> , 106: 270-276 (1998).		
149.	Gish, D. T. et al., "Nucleic Acids. 11. Synthesis of 5'-Esters of 1-.beta.-D-Arabinofuranosylcytosine Possessing Antileukemic and Immunosuppressive Activity," <i>J. Med. Chem.</i> , 1971, 14(12): pp. 1159-1162.		
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	156.	King et al.; "Preparation of Protein Conjugates with Alkoxypropylene Glycols" <i>Int. J. Peptide Protein Res.</i> 16 147-155 (1980).	
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Jeffrey E. Russell

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June 2, 2003

Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.